pain when applied over an inflamed organ, *e. g.*, an appendix or gall-bladder.

4. Evidences of respiratory infection are usually present in diaphragmatic pleurisy, such as cough, expectoration, herpes of lips, sore throat, high leukocytosis, rapid respiration, etc.

5. Appearance of a sharp, definitely localized pain in the neck on the same side as the abdominal pain often reveals the true condition, since it points to irritation of the phrenic nerve.

6. The referred pains in the neck and abdomen are usually induced or aggravated by cough and deep inspiration.

7. Nausea and vomiting are more constant in visceral abdominal inflammation, but may occur and be very pronounced also in diaphragmatic pleurisy.

8. Hiccough is not a common symptom in diaphragmatic pleurisy, contrary to the current belief. It was present only five times in our series of sixty-one cases. It is more often seen in visceral diseases of the abdomen than in diaphragmatic pleurisy.

SUBPHRENIC INFLAMMATION. In the study of pain distribution from subphrenic inflammation, we are greatly handicapped. The opportunities for experimental irritation of the under surface of the diaphragm in human beings are rare. Moreover, the existence of abdominal pain in the course of subphrenic inflammation may be properly attributed to associated inflammation of the abdominal viscera. Only in those cases in which definite, sharply localized pain and tenderness develop in the neck or shoulder region, can we be sure that the diaphragm is involved. We have collected six cases of subphrenic inflammation exhibiting neck pain, three on the left side and three on the right. The painful point is in every respect identical with the referred pain in diaphragmatic pleurisy.

The nerve supply of the peritoneal covering of the diaphragm is probably the same as that of the pleural surface, that is to say, the lower intercostal nerves supply the outer margin, and the phrenic nerves supply the central portion. Hence it is impossible to differentiate between supraphrenic and subphrenic inflammation by the pain alone. The symptomatology and physical findings must also be considered, in order to establish the diagnosis.

THE CEREBRAL NERVE DISTURBANCES IN EXOPHTHALMIC GOITRE.

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THE cerebral disturbances which occur in exophthalmic goitre are among the rarer manifestations of this remarkable disease. Headache, often intense, is a very common symptom, as are

irritability, emotional outbursts, and disturbances in sleep with terrifying dreams. Graver associated conditions may occur, such as neurasthenia, hysteria, and the various psychoses, such as manic-depressive insanity, melancholia, dementia precox, paranoia, and acute delirium. Organic cerebral changes giving rise to convulsions, epilepsy, and epileptiform attacks, muscular weakness, paralyses of the cerebral nerves, hemiplegias and paraplegias, anesthesias, paresthesias, and hyperesthesias may be associated with this disease.

The chief purpose of this communication is to call attention to one group of these cerebral disturbances, namely, the cerebral nerve palsies. In the enormous literature on Basedow's disease not more than eighty cases, including all types, are recorded, the great majority of which have been observed in European clinics. Only four cases appear in American literature (Campbell Posey, Dana, Gordon, Bartholow). At the Johns Hopkins Hospital, among more than 300 cases of exophthalmic goitre occurring in the service of Dr. Halsted, the case to be reported is, with the exception of an occasional mild grade of ptosis, the first instance which has come under observation.

The cerebral nerves affected are most commonly those controlling the movements of the eyes and lids, but a review of the literature shows that almost every cerebral nerve has been involved, either alone or in combination with other nerves. Least common is the group of cases with an associated bulbar paralysis, of which perhaps only ten have been reported. The case to be described is of this group.

The patient, a Russian Jew, aged twenty-three years, a recent graduate in medicine, was admitted to the surgical service of the Johns Hopkins Hospital January 31, 1911, complaining of weakness, vomiting, shortness of breath, difficulty in swallowing, and double vision. The family history is unimportant. The mother is in rather poor health and nervous. There is no history of exophthalmic goitre in other members of the family. The patient has always been delicate and of a nervous temperament, but has not had any severe illnesses. He was admitted to the medical service of the Johns Hopkins Hospital December 17, 1907, complaining of weakness and vomiting. The history which he gave at that time was as follows:

Two years before (in 1905) he had an attack of vomiting lasting for a few days; a year later he had a second similar attack; the third attack (for which he was admitted to the medical service) had been of two months' duration, and had increased in severity so that even small amounts of milk could not be retained. He had lost thirteen pounds in weight in the week immediately preceding his first admission. The vomiting had not been associated with nausea or pain; the food ingested was expelled without effort

or distress. During the few days before admission he had had diarrhea, four to five movements daily. Examination at that time (in 1907) showed an emotional, nervous young man with normal pulse and temperature; no exophthalmos or characteristic eye signs, apparently no enlargement of the thyroid gland, and no cerebral nerve disturbances. The lungs were clear; there was a faint systolic blow at the apex of the heart; the abdomen was negative. Acetone and diacetic acid were present in the urine. Dr. Barker noted, at this time, pigmentation of the skin and the absence of axillary hair. The patient remained in the hospital but two days, at the end of which time he insisted upon going home.

Present Illness (January 31, 1911). The patient states that he was perfectly well until March or April, 1909. He then noticed a swelling of his neck, which at first was not accompanied by any symptoms. Just previous to its appearance he had been roughly handled by his fellow-students and badly frightened. The enlargement of the neck was very rapid. Three months after the first appearance of the goitre he was unable to wear a collar, and had become very nervous. Tachycardia was first noted several months after the appearance of the goitre, and has persisted, but without subjective palpitation of the heart. A year after the appearance of the goitre (1910) he became aware of a droop of the right upper lid; there followed soon a similar condition of the left lid. This bilateral ptosis has gradually become more marked, and at present the patient is quite unable to raise the lids. Soon after the appearance of the ptosis he was troubled with double vision, a condition which has persisted. About five weeks before admission, owing to loss in the power of mastication, he was unable to chew solid food. In the past month he has had difficulty in speech; he has jumbled his words and states that he has "talked through his nose." A week before admission he completely lost his voice for a period of three days. For the same period his tongue felt thick; there has been a collection of mucus in his throat; he has had frequent cough and marked subjective dyspnea. There has been difficulty in swallowing, and fluids taken by the mouth have been repeatedly regurgitated through the nose. The patient has, however, been able to attend to his medical duties until three weeks ago, when great weakness of the upper and lower limbs compelled him to give up his work.

Examination. The striking feature on inspection was the patient's facial appearance. The drooping lids, the protruding, fixed eyes, the mask-like face, the open mouth and hanging jaw made a truly striking picture (see Fig. 1). He was weak, perspired profusely, and looked ill. He was unable to raise his head from the pillow, could scarcely raise his shoulders, and only with the greatest effort lift his arms from the bed. Dyspnea was so great that he was compelled to sit up in bed. Unable to expel the mucus

which collected in his throat, he had frequent, violent paroxysms of coughing. His voice had a distinctly nasal quality. He was clear mentally, but forgetful. He was emotional, and repeatedly burst into tears without assignable cause.

The exophthalmos was extreme. The other eye signs could not be tested on account of the complete bilateral ptosis and fixation of the globes. The thyroid gland was much enlarged, the right lobe more than the left, and was fairly soft and smooth. There was marked pulsation of the entire goitre, but no palpable thrill. On auscultation, a loud, systolic bruit could be heard over the entire gland; it was loudest over the superior thyroid vessels.

FIG. 1.—The striking facial appearance; the drooping lids, protruding fixed eyes, mask-like face, open mouth, and hanging jaw.

The pulse was regular and almost constantly about 120 per minute; the blood-pressure was 120 mm. Hg. The heart was not enlarged either to the right or left. A faint systolic bruit was heard over the apex; the sounds at the base were clear. There were no edemas. There was a well-marked tremor of the fingers. The hands and feet were sweating. Pigmentation was pronounced, particularly over the flexor and extensor surfaces of the extremities and about the trunk. Over the lower legs were several more or less circumscribed, brownish areas, and around the ankles there was quite a definite band of pigmentation. The skin of the abdomen was dark, especially about the waist line, where it was coffee-colored. There was some pigmentation of the skin of the forehead, deep

pigmentation about the genitalia, but none of the mucous membranes of the mouth.

Nausea, vomiting, and a rather persistent diarrhea, complained of during his illness, were absent during his stay in the hospital.

Blood Examination. Red cells, 5,600,000; hemoglobin, 100 per cent.; white cells, 9000; polymorphonuclears, 71 per cent.; eosinophiles, 1 per cent.; large mononuclears, 10 per cent.; small lymphocytes, 12 per cent.; large lymphocytes, 2 per cent.; transitionals, 2 per cent.

Examination of the lungs and abdomen was negative.

In the urine there was a trace of albumin in two of the four specimens examined and a well marked acetone reaction in three of them. Wassermann reaction was negative.

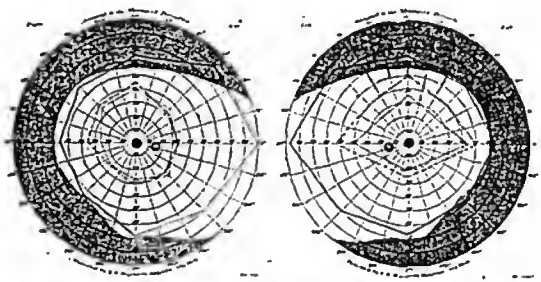

FIG. 2.—The eye fields, showing normal form fields, but contraction of the color fields, with interlacing of colors in right eye.

Cerebral Nerves. No disturbance in smell could be demonstrated. Taste also appeared to be fairly normal, although he miscalled salty and acid substances. There was complete bilateral ptosis of the eyelids. At rest the lids covered more than the upper half of either cornea. With the greatest effort the left upper lid could be raised slightly, but this movement seemed to be due rather to the elevation of the left eyebrow than to a true movement of the lid. The right upper lid could not be raised at all.

The greatly protruding eyes were practically fixed; there was no lateral, vertical, or rotary motion on either side. This total lack of movement of the globes persisted until the patient's death. Both eyes were directed forward in almost parallel lines. Double vision was constant, the upper image being the false one. Movements of the head from side to side had no influence on the position of the eyeballs, this test indicating an infranuclear rather than a supranuclear involvement. There was, therefore, a complete

ophthalmoplegia externa, a complete paralysis of the III, IV, and VI cerebral nerves. The pupils were usually but not constantly unequal in size, the left being larger than the right. They reacted promptly to light. The fundi were normal. The eye fields (see Fig. 2), showed normal form fields, but contraction of the color fields with interlacing of colors in the right eye.

The sensory fifth nerve appeared to be unaffected. There was no anesthesia of the conjunctiva and no sensory disturbance in the area of distribution of the trigeminal on either side of the face. The motor fifth, however, seemed markedly involved. The open mouth and hanging jaw were apparently due to the weakness of the muscles supplied by this nerve. At times the patient was unable to close the mouth; at other times he could, with a great effort, bring the teeth together. There was no evidence of contraction or atrophy of the masseters.

Nerve VII. Facial weakness was manifest on both sides, being more marked on the right than on the left. The face appeared placid and mask-like. The ordinary expressional movements were feebly executed. The patient could at times pucker his lips slightly and draw down the angle of the mouth; he was able to elevate the left eyebrow but not the right.

No disturbances in hearing could be demonstrated by the ordinary tests.

The voice, thick and indistinct, had decidedly a nasal quality; there was difficulty in articulation but no aphasia. The patient stated that his tongue felt stiff and awkward. Swallowing was difficult, and fluids taken by the mouth were in part regurgitated through the nose. There was a constant collection of mucus in the throat, which the patient seemed unable to expel. Cough was frequent and violent. Dyspnea was marked. The patient was able to protrude his tongue but slightly and the lingual movements were awkwardly performed. There was a marked tremor of the tongue. Examination of the palate and the pharynx was difficult. The palate appeared symmetrical. The pharyngeal muscles could be seen to move, but the examination was unsatisfactory. Sensation of the pharynx appeared to be normal. Examination of the larynx was unsatisfactory because of the patient's restlessness and the presence of mucus in the throat. Dr. Crowe stated the cords moved well on phonation.

The trapezius muscles were weak, the patient being hardly able to elevate his shoulders. Atrophy of these muscles was not demonstrable.

Paracentral Region. There were no gross sensory disturbances on either side of the body. There was, however, marked hyperesthesia of the skin. The patient complained whenever the skin was touched. This sensitiveness seemed especially pronounced over the abdomen and legs. The soles of the feet were extremely

sensitive, and the patient objected bitterly whenever plantar stimulation was attempted. There was no definite paralysis of the extremities, but a profound, general weakness. As has been stated, the patient was unable to support his head or to elevate his shoulders, he was barely able to raise his arms from the bed. The grip in either hand was practically *nil*. The muscular power in the legs was distinctly greater than in the arms. The muscular weakness seemed greater upon the right than upon the left side.

The reflexes were active at the knees and ankles. A suggestive ankle-clonus was obtained on one occasion. Plantar stimulation was unsatisfactory because of the extreme sensitiveness of the soles of the feet. The abdominal and cremasteric reflexes were normal. To Oppenheim's test there was a normal response.

Summary of Neurological Findings. Complete bilateral ptosis, complete ophthalmoplegia externa, paralysis or at least marked paresis of the motor fifth and of the seventh, bulbar paralysis, hyperesthesia of the skin, and profound muscular weakness.

Symptoms Referable to Involvement of Ductless Glands Other Than the Thyroid. The great muscular weakness, the pigmentation of the skin, and diarrhea suggested possible involvement of the *thymus* and *adrenal glands*. The pigmentation was most marked in places of pressure, that is, along the waist line, about the shoetops, and around the neck.

Symptoms suggestive of involvement of the *hypophysis* were also present. The body was quite fat, with a thick panniculus. The skin was soft, smooth, and feminine in appearance. The hips were rather broad. There was almost complete absence of axillary hair; the beard was less abundant than normal and there was absence of hair over the forearms and backs of the hands. The genitalia appeared to be normal. During the two months previous to admission there had been complete absence of all sexual desire.

Given the neurological findings which have been described, the question arose, Were we perhaps dealing with an organic lesion or lesions in the brain or with a myasthenia gravis? The picture presented by the patient corresponded closely with myasthenia gravis, which indeed has been observed associated with exophthalmic goitre. In that disease there may be ptosis, involvement of the eye muscles, the muscles of the face, of mastication, etc. All the voluntary muscles may become involved. Myasthenia gravis has been fatal in about 40 per cent. of the cases. Examination of the nervous system in this disease has revealed no abnormality. Of value in differential diagnosis is the myasthenic reaction of Jolly, the rapid exhaustion of the muscles by faradism. Our patient was tested for the myasthenic reaction on three successive days. Faradic stimulation sufficient to produce a good contraction of the muscles was employed. The muscles tested were usually the facial, the deltoid, and the quadriceps extensor of the leg. The stimuli were

applied at the rate of about 1 per second, and in all cases at least one hundred times, and sometimes for from two to five minutes. In none of the examinations could any fatigue of the muscles be demonstrated even after repeated stimuli. If this test is of value our patient was not a case of myasthenia gravis.

The patient remained in the hospital for six days. He refused operation. He was visited at his home, and in the ten days which elapsed between his first and second admissions there was no change in his condition. He finally consented to an operation, which was performed February 16, 1911, by Dr. Halsted. The condition of the patient was so serious that ligation of the superior thyroid arteries alone was done. Anesthetization was begun with the patient in a sitting position because of the orthopnea. His pulse rose to 170, and at one time to 180 during the operation, but at the end of the procedure his condition was satisfactory.

Postoperative Course. The patient was again carefully examined between eight and ten hours after operation. There was subjective improvement, the patient stating that he felt better than before the operation. Some slight movement of the globes was demonstrable, but this was not striking. His pulse was about 140. His temperature had risen to 101°. There had been some nausea following operation, but very little vomiting. He passed a fair night. During the following day (February 17) his pulse remained about the same, although at times it was slightly irregular. His temperature remained elevated. His blood-pressure, about 120, was unaffected. He eagerly took water, but the greater part of it was promptly expelled through the nose. There was a constant collection of mucus in the throat and frequent choking spells. About 8 P.M. of this day he complained greatly of shortness of breath, and became choked with mucus which he was unable to expel. His respirations suddenly ceased at 10 P.M., the heart continuing to beat. With the idea that there might be some obstruction to respiration a tracheotomy was promptly performed and artificial respiration undertaken. The heart continued to beat for perhaps five minutes during this procedure, and then ceased. Death, therefore, seemed to be due to an acute respiratory paralysis. Certainly, it was not a cardiac death, as is so often the case in exophthalmic goitre.

Most unfortunately an autopsy could not be obtained. A fragment of the thyroid gland, however, was removed, which showed the histological picture of Basedow's disease.

LITERATURE. The literature on cerebral nerve disturbances in exophthalmic goitre up to and including the year 1911 is considered with remarkable comprehensiveness by Sattler and Kappis. From these two authors chiefly and from the literature since 1911, I have obtained the following data as to the frequency of involvement of the various cerebral nerves.

1. Isolated palsies of the first or olfactory nerve have not been

reported in the literature, nor have isolated disturbances in taste. In combination with other cerebral nerve disturbances, loss of smell and taste has been observed in two cases of exophthalmic goitre (the cases of Warner and Bristow and of Ballet).

II. Isolated loss of vision has not been reported in exophthalmic goitre. Combined with other cerebral nerve disturbances the optic nerve has been affected in one case (Ballet), which showed diminished visual acuity on the left side with contraction of the visual field.

III. The third or oculomotor nerve has been most frequently affected and the majority of the cases reported have shown involvement of this nerve. Single muscles or all the muscles supplied by this nerve have been involved. Levator palsies and ptosis, either unilateral or bilateral, have been observed as isolated findings 9 times. Isolated rectus superior palsies have been reported 6 times and isolated rectus internus or convergence palsies 7 times. Of the latter, some observations seem questionable. Combined with other cranial-nerve disturbances the III nerve has been frequently affected. Isolated ophthalmoplegia externa, that is to say, palsy of the III, IV, and VI nerves, has been reported 6 times and an ophthalmoplegia externa combined with bulbar paralysis, as in our case, has been observed 5 times. The nerves supplying the internal muscles of the eye, *i. e.*, the pupils, have been affected in 5 instances.

IV. Isolated palsy of the fourth or trochlear nerve has been reported in one case; combined with other nerve lesions in 13 or 14 cases.

V. Isolated palsy of the motor fifth has not been observed; combined, this nerve has been affected 5 times, chiefly in cases of bulbar palsy. Involvement of the sensory fifth has not been reported except associated with a hemianesthesia.

VI. The VI nerve has, next to the III, been most frequently affected. Isolated palsy of this nerve has been observed 10 times. It has been frequently involved associated with the palsies of the III and IV nerves in opthalmoplegia externa and in the cases with bulbar paralysis.

VII. Isolated palsies of the VII or facial nerve have occurred 5 times; combined with other cranial nerve disturbances 8 times.

VIII. Isolated involvement of the auditory nerve has not been reported. Combined with other disturbances loss of hearing has been noted in one instance.

IX. Isolated palsy of the glossopharyngeal nerve has been observed once. Combined, it has been involved in association with other nerves in the cases with bulbar paralysis.

X. The pneumogastric has not been affected alone. Vagus disturbances, however, have occurred in the cases with bulbar paralysis.

XI. The spinal accessory appears to be the only cranial to have escaped involvement in exophthalmic goitre. No true palsy of this nerve has been recorded either isolated or combined. Marked weakness of the sternomastoid and trapezius muscle has been observed in association with general muscular weakness, as in our case.

XII. Isolated palsy of the XII nerve has not been reported. Combined, this nerve has been involved in the cases with bulbar paralysis.

It may be seen from this brief summary that the nerves controlling the eye muscles are most frequently involved in exophthalmic goitre. Kappis was able to collect over 40 cases in which the eye muscles alone were affected. Isolated palsies may occur, but combinations of various kinds are most commonly seen. A pure ophthalmoplegia externa, as previously stated, has been observed in 6 cases.

With the exception of palsies of the facial, 5 cases of which have been reported, isolated palsies of the remaining cerebral nerves are extremely rare. Combined palsies of these nerves, as recited, are not uncommon, and the most varied clinical pictures occur.

The cases with bulbar paralysis form a most interesting group, and deserve perhaps more than passing mention. They have all been severe cases of exophthalmic goitre, and in most instances the disease has run a rapid course. In one instance the patient had had a goitre for many years, on which Basedow had become engrafted.

The duration of the disease has varied from a few days to five or six months before the onset of bulbar symptoms. Death has invariably followed the appearance of these symptoms, and in the majority of instances within a short time. One case died one day, another three days, and another eight days after the onset of bulbar symptoms, while others have lived from several weeks to three months thereafter. We may, therefore, divide the cases into those with acute (the majority) and those with chronic bulbar palsy. Our case is of the latter group. While there has been considerable variety of combination in the nerve palsies, the bulbar symptoms have been remarkably uniform in all the cases.

It is difficult, from the reports of cases in the literature, to differentiate the cases of bulbar paralysis due to organic lesion from those of myasthenia gravis with bulbar symptoms; and it is possible that some of the 12 cases assigned to true bulbar palsy do not correctly belong in that group. The cases were all reported between 1886 and 1904, and 8 of them before 1900. The myasthenic reaction was tested, apparently, in very few instances, if at all. We have, therefore, to base our opinion largely on the clinical course of the paralysis. Autopsy findings are suggestive but not altogether convincing. In 6 of the 12 cases an autopsy was not done, or no mention is made of it. In 4 of the remaining 6 cases a definite

lesion was found in the nuclei of the affected nerves, described either as an area of softening or of fresh encephalitis. In the remaining 2 cases it is stated that gross lesions of the brain were not present; but serial sections for microscopic examination were not made, and therefore these negative findings are inconclusive; 2 of the 12 cases certainly suggest a myasthenia gravis chiefly because of the variability in the palsies. In neither of these 2 cases was an autopsy obtained.

ETIOLOGY OF NERVE PALSIES IN EXOPHTHALMIC GOITRE. As regards the etiology of nerve palsies in exophthalmic goitre, it may be said that no very definite knowledge is at hand. It is assumed that the disturbances in the cerebral nerves are of a toxic nature, the toxins being responsible for the lesions in the nuclei of the cerebral nerves. Clinically, there is some evidence for this assumption, for palsies occur, as a rule, after the disease is well established, and never, so far as is known, in cases of cured exophthalmic goitre. Cases are known, however, though they are very rare, in which palsies appeared shortly before the outspoken symptoms of Basedow's disease, while in a few instances the palsies and the usual symptoms of exophthalmic goitre have appeared simultaneously.

PATHOLOGY. In 4 of the 6 cases with bulbar paralysis in which autopsies were obtained, definite lesions were present in the medulla associated with extensive degeneration of fiber tracts. The 2 cases with negative findings are not conclusive, for a careful examination of the brain was not made. It has been in the cases with bulbar paralysis that the most positive pathological findings have been obtained, for they have all been severe cases of exophthalmic goitre which have quickly terminated fatally. In the great majority, the palsies have affected chiefly the eye muscles and apparently have not influenced greatly the course of the disease. These cases have gone from observation and the end result has not been known. In brief, it may be said that comparatively few pathological lesions in the brain have been recorded in the cases of exophthalmic goitre with nerve palsies. This may perhaps be explained (1) by the fact that they rarely have been looked for, (2) because the majority of the patients have not died while under observation, and (3) because serial sections of the brain have not been made—a necessity for the demonstration of a small lesion.

THE CLINICAL COURSE OF THE CEREBRAL NERVE PALSIES. The palsies may appear at any stage of the disease. In most cases they manifest themselves months or even years after the onset of the disease; in one case it was not until six years after the first symptoms of exophthalmic goitre that the palsies were noted. They may, however, begin acutely, simultaneously with or soon after the other symptoms. In a few instances the palsies have been reported as the first symptom of Basedow's disease. In most cases they

have entered the clinical picture almost unobserved, the disease not having become noticeably more serious with their occurrence. But the palsies may, as stated above, begin acutely and spread rapidly. In some of the cases reported it has developed over night, and synchronous with the rapidly spreading palsies there has been a marked increase in the severity of the disease.

In cases in which several nerves were involved there seems to have been no uniformity as to the order in which the paralysis appeared. Frequently they have occurred almost simultaneously, but they may follow one another at irregular intervals. The period between the onset of the first palsy and that of the last has not been great—less than a year in the vast majority of cases, but two years in a patient of Kappis. The complete paralyses have usually persisted unchanged. In no case has the palsy been benefited by operation, although marked improvement in other symptoms has been noted. There are apparently 2 cases, however, in which palsies of short duration have disappeared on improvement of the other symptoms, and 3 cases in which there was a partial recovery of the palsies.

What has been said thus far regarding the clinical course of these palsies does not hold for the cases with bulbar paralysis. These cases have, without exception, been highly toxic, the palsies have been rapidly progressive, and a fatal termination has quickly followed.

Differential Diagnosis. I shall merely mention some of the conditions in exophthalmic goitre which may simulate the true palsies. As has been said, myasthenia gravis undoubtedly may be associated with this disease. Sattler gives abstracts of 6 cases in which a positive myasthenic reaction was obtained. In addition to the myasthenic reaction a fairly characteristic finding in the cases of myasthenia is the variation from day to day in the palsies. Brain tumor has been noted in one case of exophthalmic goitre with nerve palsiess. Cerebral hemorrhage, multiple neuritis, and multiple selerosis have all been observed associated with exophthalmic goitre, and it is possible that these complications might give rise to some difficulty in diagnosis.

Prognosis. A few additional words may be said as to the prognosis in the cases of Basedow with nerve palsies. Slight palsies, as those of the eye muscles, such as occur in the majority of the cases do not necessarily make the prognosis more grave. The paralyses themselves do not lead to death; the prognosis depends, as I have said, upon the severity of the Basedow. If the paralyses develop slowly, or acutely if merely to a slight extent, they have a serious significance *per se* only when they involve important nerves such as the vagus, which occurred in one case of Kappis. In the cases with very acutely developing and at the same time extensive paralyses the development of a bulbar paralysis is to be feared.